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74476                      7590                      05/27/2011 Nestle HealthCare Nutrition 12 Vreeland Road, 2nd Floor, Box 697 Florham Park, NJ 07932				
EXAMINER				
HA, JULIE				
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**BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES**

Application Number: 10/580,186  
Filing Date: September 21, 2007  
Appellant(s): BRENNISEN ET AL.

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Robert M. Barrett  
For Appellant

**EXAMINER'S ANSWER**

This is in response to the appeal brief filed April 20, 2011 appealing from the Office action mailed November 24, 2010.

**(1) Real Party in Interest**

The real party in interest in the case is Universitat Bern by virtue of Assignment dated September 21, 2007, the assignee of record.

**(2) Related Appeals and Interferences**

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

**(3) Status of Claims**

The following is a list of claims that are rejected and pending in the application:  
Claims 10, 12-24, 26-28, 38-40 and 45-47.

**(4) Status of Amendments After Final**

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

**(5) Summary of Claimed Subject Matter**

The examiner has no comment on the summary of claimed subject matter contained in the brief.

**(6) Grounds of Rejection to be Reviewed on Appeal**

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

**(7) Claims Appendix**

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

**(8) Evidence Relied Upon**

Muhlbauer, WO 98/50054 A (Nov 12, 1998).

Kuttan R, "The isolation and characterization of gamma-L Glutamyl-S-trans-1-propenyl-L cysteine sulfoxide from Sandal Santalum-Album an interesting occurrence of sulfoxide diastereoisomers in nature" Biochemistry, vol13, no. 21, 1974, pp. 4394-4400.

Wetli, HA. "A gamma-glutamyl peptide isolated from onion (*Allium cepa* L.) by bioassay-guided fractionation inhibits resorption activity of osteoclasts" J. Agric. Food Chem., vol59, no. 9, 2005, pp.3408-3414 (abstract only).

**(9) Grounds of Rejection**

The following ground(s) of rejection are applicable to the appealed claims:

Claims 10, 12-24, 26-28, 38-40 and 45-47 stand rejected under 35 U.S.C. 102(b) as being anticipated by Muhlbauer (WO 98/50054, filed with IDS) as being evidenced by Kuttan et al (Biochemistry, 1974, 13(21): 4394-4400, filed with IDS) and as evidenced by Wetli et al (J. Agric. Food Chem., 2005, 53(9): 3408-3014, abstract only provided in the previous office action and full article provided herein).

Muhlbauer reference teaches a nutritional composition comprising all of the active components of instant claims (see throughout the reference, Claims 5-20), meeting the limitation of instant claims 10 in part, 38 and 45. The reference teaches that the nutritional or pharmaceutical compositions containing a plant extract or concentrate selected from the group consisting of allium, eruca, petroselinum and brassica extracts or concentrates (see abstract and p. 2, last paragraph). The reference teaches that the composition is useful for the treatment of diseases or conditions which are characterized by increased bone resorption, osteoporosis (see abstract). The reference teaches that the term allium refers to the genus allium and includes for example any member of the botanical species *Allium cepa* (onion), *Allium ascalonium* and so on, and indicates that the preferred extract is from *Allium cepa* (see p. 3, 2<sup>nd</sup> paragraph, see p. 4, 6<sup>th</sup> paragraph). The onion extracts and concentrates are prepared from the whole eatable part of the vegetable (see p. 3, 3<sup>rd</sup> paragraph). The reference teaches that the extract and concentrates of the above-mentioned plants or vegetables may be in liquid

form or in solid form such as in granulate or powder form (see p. 5, 1<sup>st</sup> paragraph), meeting the limitation of claims 22-23. The reference teaches that suitable methods of obtaining extracts of the above-mentioned plants or vegetables are known in the art...by extracting the fresh cut or dried plants or vegetables or the respective roots, fruits or seeds thereof for example with water or with one or more food grade solvents or with a mixture of water and one or more food grade solvents...ethanol (see p. 5, 3<sup>rd</sup> paragraph). Further, Example 4 at page 16, explicitly teaches ethanol/water extraction. As evidenced by Kuttan et al,  $\gamma$ -L-glutamyl-S-(trans-l-propenyl)-L-cysteine sulfoxide isolated from sandal (*Santalum album* L.) is the same as the protein isolated from onion (*Allium cepa*) (see abstract). The reference teaches that  $\gamma$ -L-glutamyl-S-(trans-l-propenyl)-L-cysteine sulfoxide is in aqueous solutions, water (see p. 4396, right column, "CD Absorption"). Therefore, the ethanolic extract of allium cepa of the reference would inherently comprise the  $\gamma$ -L-glutamyl-trans-S-l-propenyl-L-cysteine sulfoxide of the instant claims. The reference teaches that the extract may be used in liquid form, particularly in aqueous form, or in solid form, granulate or powder form. If the extracts in liquid form, it has a solid contents of for example from 1 to 25% by weight, preferably from 2 to 20% by weight and most preferred from 2 to 15% by weight (see p. 6, 2<sup>nd</sup> paragraph).

The reference teaches that the subject to be treated is an adult person a satisfactory inhibitory effect on bone resorption is, in general obtained with compositions formulated to allow a daily administration of 0.1 to 20 grams, preferably 0.2 to 15 grams and most preferred 0.4 to 10 grams of allium, petroselinum, brassica and/or eruca

concentrate or extract (see p. 6, 2<sup>nd</sup> paragraph). The reference further teaches that suitable nutritional compositions comprising the plant/vegetable extracts comprise at least one (a) plant/vegetable extract or concentrate from allium, (b) a calcium source, and (c) at least one energy source selected from carbohydrate, fat and nitrogen sources, and Vitamin D (see p. 6, last paragraph, claim 5), meeting the limitation of instant claims 10, 12, 38 and 45. Since the nutritional composition comprises the same active compound, this would inherently have the same functionality and characteristics of instant claims 38 and 45. The reference teaches that from approximately 0.1 to 40%, preferably from approximately 3 to 25% of plant/vegetable extract or concentrate component (a) (see p. 6, last paragraph); calcium source such as calcium chloride or skim milk and the calcium source (b) is in one unit dosage from about 100 mg to 1000 mg, preferably 200 mg to 700 mg or from approximately 1 to 60 %, preferably from approximately 5 to 50% of calcium component (b) (see p. 7, 1<sup>st</sup> and 2<sup>nd</sup> paragraph); suitable carbohydrate sources include for example maltodextrins, starch, lactose, glucose (see p. 7, 3<sup>rd</sup> paragraph); suitable fat sources include omega-6 polyunsaturated fatty acid (see p. 7, 4<sup>th</sup> paragraph); suitable nitrogen sources such as soybean derived proteins (see p. 8, 4<sup>th</sup> paragraph), meeting the limitation of claims 14-17 and 19. The reference teaches that the nutritional composition comprise from approximately 0.1 % to 98.9%, preferably from approximately 1 to approximately 95% of energy source (p. 9, 1<sup>st</sup> paragraph), further meeting the limitation of claim 19. The reference teaches that the carbohydrate source provides for 30 to 70% of the total energy supply, the nitrogen source for 5 to 45 %, and the fat source for 0.1 to 15% of the total energy supply (see p.

9, 2<sup>nd</sup> paragraph), meeting the limitation of instant claim 18. Further, the reference teaches that the nutritional formulation may comprise other nutritionally acceptable components such as vitamins (see p. 10, 1<sup>st</sup> paragraph), meeting the limitation of instant claim 20. The reference teaches that the supplement comprises energy sources in an amount supplying from 50 to 1500 kcal/day (see p. 11, 2<sup>nd</sup> paragraph, see claim 16), meeting the limitation of instant claim 21. The reference teaches that the nutritional formulation is formulated in any form suitable for enteral administration, in aqueous form or in powder or granulate form, whereby the powder or granulate is conveniently added to water prior to use (see p. 11, 1<sup>st</sup> and 2<sup>nd</sup> paragraphs), meeting the limitation of claims 24 and 26. Additionally, the reference teaches dragee, table, capsule, sachet or suppository compositions (see p. 12, 3<sup>rd</sup> paragraph, see claim 20), meeting the limitation of instant claims 27-28.

Furthermore, the reference teaches that 250 mg freeze-dried onion extract are obtained for each g of dry whole onion, and the onion extract (0.017, 0.17, 1.7 mg onion extract/ ml medium) inhibited osteoclast-mediated resorption (see column 12, lines 1-9). As evidenced by Wetli et al, the molecular mass of gamma-L-glutamyl-trans-S-1-propenyl-L-cysteine sulfoxide is 306 Da (see abstract). The onion extract at 0.017 mg/ml would yield 55.5  $\mu$ M effective dose; at 0.17 mg/ml would yield 555.5  $\mu$ M effective dose; at 1.7 mg/ml would yield 5.55 mM effective dose, meeting the limitation of instant claims 39-40 and 46-47. Therefore, the reference anticipates instant claims 10, 12-24, 26-28, 38-40 and 45-47.



**(10) Response to Argument**

***Response to Appellant's Arguments***

Appellant argues that "Independent claims 10 and 24 recite, in part, nutritional and pharmaceutical compositions, respectively, comprising a  $\gamma$ -glutamyl peptide selected from the group consisting of  $\gamma$ -glutamyl-alkyl-cysteine sulfoxide,  $\gamma$ -glutamyl-alkenyl-cysteine sulfoxide, and combinations thereof, a carrier and a fat source. Appellant has surprisingly found that the active constituent of allium responsible for the bone resorption inhibiting effect may be found in a hydrophilic, ethanolic extract of allium such as allium cepa. The active constituent having a potent inhibitory effect on bone resorption was identified as  $\gamma$ -glutamyl peptide selected from the group consisting of  $\gamma$ -glutamyl-alkyl-cysteine sulfoxide,  $\gamma$ -glutamyl-alkenyl-cysteine sulfoxide  $\gamma$ -glutamyl peptide, for example a  $\gamma$ -glutamyl-alkyl-cysteine sulfoxide or  $\gamma$ -glutamyl-alkenyl-cysteine sulfoxide or  $\gamma$ -L-glutamyl-alkyl-trans-S-1-propenyl-L-cysteine sulfoxide."

Appellant argues that "the disclosure of a large genus rarely anticipates a narrowly claimed species." Appellant further argues that "although Muhlbauer discloses the genus allium and mentions *allium cepa*, Muhlbauer fails to anticipate the present claims because the genus *allium cepa* is too large for the skilled artisan to envisage a  $\gamma$ -glutamyl peptide extracted from *allium cepa*, let alone a specific  $\gamma$ -glutamyl peptide selected from the group consisting of  $\gamma$ -glutamyl-alkyl-cysteine sulfoxide,  $\gamma$ -glutamyl-alkenyl-cysteine sulfoxide, and combination thereof as required, in part, by currently amended independent claims 10 and 24.

Appellant further argues that "Further, Kuttan and Wetli fail to disclose or suggest nutritional and pharmaceutical compositions, respectively, comprising a  $\gamma$ -glutamyl peptide selected from the group consisting of  $\gamma$ -glutamyl-alkyl-cysteine sulfoxide,  $\gamma$ -glutamyl-alkenyl-cysteine sulfoxide, and combination thereof, a carrier, and a fat source as required, in part, by independent claims 10 and 24.

Appellant argues that "Kuttan expressly states that 'circular dichroism measurements established that the sulfoxide group in the sandal and onion peptides are of opposite configurations. The skilled artisan would immediately appreciate that stereoisomers of the same compound can have widely varying properties.'"  
Appellant argues that "Wetli is cited by the Examiner solely for the molecular mass of gamma-L-glutamyl-trans-S-1-propenyl-L-cysteine sulfoxide. Further, anticipation is a factual determination that "requires the presence in a single prior art disclosure of each and every element of a claimed invention."

Appellant's arguments have been fully considered but have not been found persuasive. The reference teaches all of the active components of instant claims. Muhlbauer reference teaches that the nutritional or pharmaceutical compositions containing a plant extract or concentrate selected from the group consisting of **allium**, **eruca**, **petroselinum** and **brassica** extracts or concentrates. The reference teaches that the composition is useful for the treatment of diseases or conditions which are characterized by increased bone resorption, osteoporosis. The reference teaches that the term **allium** refers to the genus **allium** and includes for example any member of the botanical species **Allium cepa (onion)**, **Allium ascalonium** and so on, and indicates

that the preferred extract is from **Allium cepa**. The reference teaches that the extract and concentrates of the above-mentioned plants or vegetables may be in liquid form or in solid form such as in granulate or powder. The reference teaches that suitable methods of obtaining extracts of the above-mentioned plants or vegetables are known in the art...by extracting the fresh cut or dried plants or vegetables or the respective roots, fruits or seeds thereof for example **with water or with one or more food grade solvents or with a mixture of water and one or more food grade solvents...ethanol**. Example 4 at page 16, explicitly teaches ethanol/water extraction. The reference teaches that the preferred plant is *allium cepa*.

The instant specification discloses that "The active constituent of allium responsible for the bone resorption inhibiting effect, may be found in an hydrophilic, ethanolic extract of allium such as *Allium cepa*" (see paragraph [0012] of instant specification US 2008/0194492).

*Allium cepa* is a species of the genus allium. Therefore, *allium cepa* is not a genus as Appellant indicates. One of ordinary skill in the art would at once envisage what the species *allium cepa* encompasses. Therefore, since Muhbauer reference teaches the nutritional or pharmaceutical compositions containing a plant extract or concentrate selected from the group consisting of allium, and specifically teaches ethanolic/water extraction from *allium cepa*, this extraction would inherently comprise the  $\gamma$ -glutamyl peptides of instant claims.

Both Kuttan and Wetli references were provided as evidence to show that  $\gamma$ -glutamyl peptide is isolated from *Allium cepa*. Kuttan and Wetli reference were not

utilized as prior arts. These were only used as evidences to provide the known properties and characteristics of the extracted components from *Allium cepa*. Kuttan et al teach that  $\gamma$ -L-glutamyl-S-(trans-l-propenyl)-L-cysteine sulfoxide isolated from sandal (*Santalum album* L.) and this is a stereoisomer of the protein isolated from onion (*Allium cepa*) (see abstract). Kuttan reference teaches that sulfoxide diastereoisomer of  $\gamma$ -L-glutamyl-S-(trans-l-propenyl)-L-cysteine sulfoxide was isolated from onion (*Allium cepa*) (see p. 4394, right column). Therefore, the same  $\gamma$ -glutamyl peptide is isolated from *allium cepa* as instantly claimed. The reference teaches that  $\gamma$ -L-glutamyl-S-(trans-l-propenyl)-L-cysteine sulfoxide is in aqueous solutions, water (see p. 4396, right column, "CD Absorption"). The reference teaches the same water (hydrophilic)/ethanolic extract as the instant specification. Therefore, the water/ethanolic extract of *allium cepa* of the reference would inherently comprise the  $\gamma$ -L-glutamyl-trans-S-l-propenyl-L-cysteine sulfoxide of the instant claims. Therefore, the reference anticipates instant claims 10, 12-24, 26-28, 38-40 and 45-47.

Wetli reference was utilized to show the molecular weight of the g-glutamyl peptide isolated from *Allium cepa* L, and to calculate and/or convert the dosage amounts disclosed in the Muhlbauer reference to mM amounts.

#### **(11) Related Proceeding(s) Appendix**

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Julie Ha/

Primary Examiner, Art Unit 1654

Conferees:

/Michael G. Wityshyn/  
Supervisory Patent Examiner, Art Unit 1651

/CECILIA J TSANG/  
Supervisory Patent Examiner, Art Unit 1654